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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants:	Simon F. Williams and David P. Martin		
Serial No.:	09/661,773	Group Art Unit:	1615
Filed:	September 14, 2000	Examiner:	C. A. Azpuru
For:	*POLYHYDROXYALKANOATE COMPOSITIONS FOR SOFT TISSUE REPAIR, AUGMENTATION AND VISCOSUPPLEMENTATION*		

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY BRIEF

Sir:

This is an appeal of the final rejection of claims 1-17 and 29-32 in the Office Action mailed September 18, 2002, maintained in the Advisory Action mailed January 15, 2003, in the above-identified patent application. A Notice of Appeal was mailed on January 21, 2003. An Appeal Brief was filed April 7, 2003. An Examiner's Answer was mailed June 18, 2003. The following remarks are in response to the Examiner's Answer.

(2) RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences known to appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

However, there are two divisional applications, both issued, U.S. Patent No. 6,598,994 and 6,555,123.

(4) STATUS OF AMENDMENTS

The claims were amended in the Amendment mailed July 25, 2002.

The Appeal Brief improperly refers to a "proposed amendment" at page 12, paragraph 4, and attaches as Appendix II and III, proposed amendments. These amendments were submitted in error and should be discarded. Paragraph 4 on page 12 should be disregarded.

(6) ISSUES ON APPEAL

The issue presented on appeal are:

(1) whether claims 1-17 and 29-32 are anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 6,277,413 to Sankaram ("Sankaram").

Note that there is an error at the top of page 3 of the Examiner's answer - the rejection is under 35 U.S.C. 102(e), not under 35 U.S.C. 102(b).

(8) ARGUMENTS

a. The Claimed Elements

The claims in issue are drawn to a polyhydroxyalkanoate for use in tissue repair or augmentation. Although the examiner is correct that an intended use alone does not impart patentability, the intended use is a feature of the claimed composition. Therefore the prior art must disclose a composition suitable for the intended use in order to disclose the claimed subject matter.

1. Injectable

For example, in the field of controlled drug delivery, a polyanhydride may be used to used to form a controlled release formulation. However, polyanhydrides are not suitable for

pharmaceutical use unless they have been recrystallized and purified to remove solvent residue and incomplete reaction products.

In the present case, the formulation contains a polymer, a polyhydroxyalkanoate, in a fluid form which is injectable. The standards developed by the Food and Drug Administration for what is injectable are stringent - the material must not be carcinogenic, inflammatory, or cytotoxic. This means that both the polyhydroxyalkanoate and the fluid base must be injectable. Particles, if present, must have a diameter of less than about 500 microns (page 10, lines 27-29), and be either in an amorphous or semi-crystalline state (page 11, lines 1-2). The material must have a viscosity of less than about 1,000,000cP to be injectable (page 10, lines 3-14).

2. Biocompatible, bioabsorbable fluid

The criteria by which the polyhydroxyalkanoate is made as a biocompatible, bioabsorbable fluid is described at page 4. There are two embodiments (page 4, lines 3-5): either a fluid at body temperature or a microdispersion (i.e., solid) in a fluid carrier. The terms "biocompatible" and "bioabsorbable" are defined at page 4, lines 14-23. Preferred polyhydroxylkanoates are waxes at room temperature or lipid polymers that do not crystallize at body temperature (page 5, lines 5-10).

3. For Repair or Augmentation of Tissue

As described in the application, materials having the properties discussed above could be used for repair or augmentation of tissue.

b. The Prior Art

The only reference the examiner has asserted is U.S. Patent No. 6,277,413 to Sankaram.

Sankaram discloses a microparticulate suspension that includes particles formed of polymer, lipids and organic solvent. Polymers are those listed at col. 3, lines 4-22. Polyhydroxyalkanoates are listed at line 6. There is no other disclosure of polyhydroxyalkanoates. Nothing is mentioned with respect to molecular weight, viscosity, crystallinity, or other properties of the polyhydroxyalkanoates required for a material for use in tissue engineering. Moreover, organic solvent is required (col. 5, lines 23-45), something the Food and Drug Administration will not allow for use in cosmetic or tissue engineering. The material is designed for drug delivery, not tissue engineering (col. 8, line 57 to col. 9, line 35). Particle size is not specified, although the particle size in the examples are between 43.6 microns (col. 12, line 62) and 7 microns (tables 2, 3, 4, 6, 8 and 9).

c. The Legal Standard for Anticipation

Under 35 U.S.C. § 102, claims are "anticipated" if a single reference, which can be an oral or written publication, that is publicly available prior to the earliest priority date, discloses each claimed element.

It must be established that a prior art reference discloses each and every element of the claims for a rejection of claims to be properly founded under 35 USC §102. *Hybritech Inc v Monoclonal Antibodies Inc*, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 US 947 (1987); *Scripps Clinic & Research Found v Genentech Inc*, 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in *Scripps*, 927 F.2d 1576:

> "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . *There must be no difference*

between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." (Emphasis added)

"A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation."

"[A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference." *Id at 1576*

For a prior art reference to anticipate a claim, the reference must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986) (citations omitted).

Regarding the issue of inherency, "[a]nticipation is a question of fact, as is the question of inherency. *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). Its proof differs from that for obviousness, 35 U.S.C. §103, in that prior knowledge by others requires that all of the elements and limitations of the claimed subject matter must be expressly

or inherently described in a single prior art reference. *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999); *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571, 7 USPQ2d 1057, 1064 (Fed. Cir. 1988). The single reference must describe and enable the claimed invention, including all claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of ordinary skill in the filed of the invention. *Crown Operations International, Ltd. V. Solutia Inc.*, 289 F.3d 1367, 1375, 62 USPQ2d 1917, 1921 (Fed. Cir. 2002); *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) ("the reference must describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the filed of the invention in possession of it.")

When anticipation is based on inherency of limitations not expressly disclosed in the assertedly anticipating reference, it must be shown that the undisclosed information was known to be present in the subject matter of the reference. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749-50 (Fed. Cir. 1991) Inherency cannot be based on the knowledge of the inventor; facts asserted to be inherent in the prior art must be shown by evidence from the prior art. *Cf. In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999)

d. The Prior Art does not disclose the claimed compositions

Claims 1 and 31 require an injectable fluid comprising a polyhydroxyalkanoate for repair or augmentation of tissue. Sankaram discloses a material for drug delivery, with no disclosure of how one could use the material that he discloses for repair or augmentation of tissue.

Sankaram's material does not inherently disclose the claimed material since it contains organic solvent, a material which is expressly not allowed for tissue augmentation, no disclosure of viscosity or other properties required to give the texture for supplementation of tissue, nor even a preference for the polymeric materials to achieve degradation over an appropriate amount of time for tissue augmentation. In summary, Sankaram does not disclose a material which is useful for tissue engineering. Sankaram, at most, discloses a huge number of materials, of which one or a few *might* be useful for tissue engineering. This is not sufficient under 35 U.S.C. 102.

Claim 2 requires the polhydroxyalkanoate be a liquid or wax at a temperature of between about 20-25C; Claims 3 and 4require the polyhydroxyalkanoate be liquid at body temperature. There is no disclosure in Sankaram of a polyhydroxyalkanoate with these properties.

Claims 5, 6, 7 and 8 require a microdispersion of particles formed of the polhydroxyalkanoate. Sankaram discloses particles of polymer, lipid and organic solvent.

Claim 9 requires particles with a diameter of less than about 5 microns. Sankaram fails to disclose particles with a diameter of less than five microns.

Claim 10 defines the monomers the polyhydroxyalkanoate must be formed of. Sankaram does not disclose any monomers forming polyhydroxyalkanoates.

Claims 11 and 12 require selection of polyhydroxyalkanoates with molecular weights of less than 100,000 and 50,000, respectively. Sankaram only discloses generic weight range, not the claimed range, and not specific for polyhydroxyalkanoates.

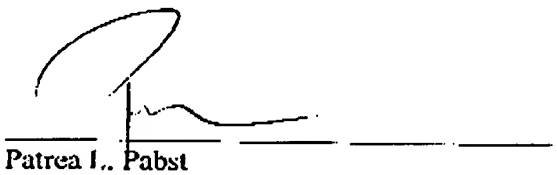
Claims 13, 14 and 29 require selection of a polyhydroxyalkanoate with a defined viscosity. Sankaram fails to disclose any viscosities, much less less for polyhydroxyalkanoates.

and even less so for use as a viscosupplement useful in treatment of knees.

Claim 30 requires selection of an amorphous polyhydroxyalkanoate. Sankaram fails to differentiate between amorphous and crystalline polymers.

In summary, Sankaram discloses the combination of a lipid and a polymer with an organic solvent, for use in drug delivery. Appellants claim a liquid polyhydroxyalkanoate formulation for use in tissue augmentation. Only with application of hindsight and ignoring the specific claim limitations could one manipulate Sankaram to say that it disclosed the claimed subject matter, either explicitly or inherently.

Respectfully submitted,



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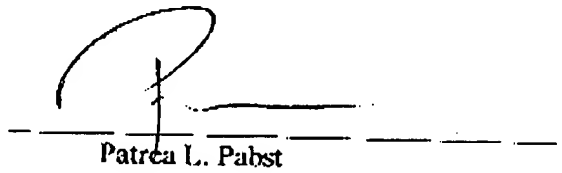

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Date: August 18, 2003

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Appendix: Claims on Appeal

1. (amended) A composition for the repair or augmentation of tissue in an animal or human, comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate which is injectable into a human or animal for repair or augmentation of tissue.

2. The composition of claim 1 wherein the polyhydroxyalkanoate is a liquid or wax at a temperature between about 20 and 25 °C.

3. The composition of claim 1 wherein the polyhydroxyalkanoate is liquid at the body temperature of the animal.

4. The composition of claim 1 wherein the polyhydroxyalkanoate is a liquid at about 37 °C.

5. The composition of claim 1 wherein the biocompatible fluid is a microdispersion of particles of the polyhydroxyalkanoate dispersed in a physiologically compatible liquid carrier.

6. The composition of claim 5 wherein the carrier is a second polyhydroxyalkanoate or an aqueous solution.

7. (amended) The composition of claim 5 wherein the particles have a diameter of less than about 500 μm.

8. The composition of claim 7 wherein the diameter is less than about 50 μm.

9. The composition of claim 8 wherein the diameter is less than about 5 μm.

10. The composition of claim 1 wherein the polymer is derived from one or more monomers selected from the group consisting of 2-hydroxybutanoate, 3-hydroxyalkanoates, 3-hydroxyalkenoates, 4-hydroxyalkanoates, 4-hydroxyalkenoates, 5-hydroxyalkanoates, 5-

hydroxyalkenoates, 6-hydroxyalkanoates, and 6-hydroxyalkenoates.

11. (amended) The composition of claim 1 wherein the polyhydroxyalkanoate has a molecular weight of less than 100,000 as determined by gel permeation chromatography.

12. (amended) The composition of claim 11 wherein the molecular weight is less than 50,000 as determined by gel permeation chromatography.

13. The composition of claim 1 having a viscosity between about 1 and 100,000 cP.

14. The composition of claim 13 having a viscosity between about 1 and 10,000 cP.

15. (amended) The composition of claim 1 further comprising a bioactive agent.

16. The composition of claim 1 further comprising a peptide or protein.

17. The composition of claim 1 wherein the polyhydroxyalkanoate is amorphous.

29. (amended) A composition suitable for use in the treatment of osteoarthritic knees comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate, wherein the composition is suitable for use as a viscosupplement.

30. The composition of claim 28 wherein the polyhydroxyalkanoate is amorphous.

31. (amended) A kit comprising

(a) the composition of claim 1; and

(b) a means for delivering the composition to a patient.

32. The kit of claim 31 wherein the means for delivering comprises a needle and a syringe.